REMARKS

Claims 23-39 were pending in the present application. Claims 23-34 and 38-39 were previously withdrawn from consideration. By virtue of this response, no claims have been cancelled or added, and claims 35 and 36 have been amended. Accordingly, claims 35-37 are currently under consideration. Amendment and cancellation of certain of the claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented.

As discussed below, the amendments to claims 35 and 36 are fully supported by the original specification. Therefore, no new matter is added.

Regarding the Drawings

The specification has been amended regarding the brief description of the drawings to clarify that Figures 1a through 1e are part of the same drawing, but that the drawing is shown on separate sheets due to its size; and that Figures 1a through 1e are referred to generically as "Figure 1." A similar amendment has been made to the brief description of the drawings with regard to Figures 2a through 2e.

As a result, it is respectfully submitted that the objection to the drawings has been suitably addressed and that no amendments to the drawings themselves are required.

Rejections under 35 U.S.C. § 112, second paragraph

The Office has rejected claims 35 and 36 as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In addition to other amendments, discussed below with respect to the 35 U.S.C. § 112, first paragraph rejection, Applicant has amended claims 35 and 36 to refer to SEQ. ID NO: 1, rather than to SEQ. ID NO. 2. This is to correct a clear clerical error. That is, these claims were previously amended to remove the explicit reference to claim 23, and claim 23 properly referred to SEQ. ID NO: 1, not to SEQ. ID NO: 2.

Rejections under 35 U.S.C. § 112, first paragraph

The Office has rejected claims 35, 36 and 37 as allegedly containing subject matter

which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention form the reasons as set forth in at pp. 3-6 ¶8-14 of the previous Office Action (Paper No. 12, 16 January 2003). While it is believed that the subject matter of these claims was fully described in an enabling manner, Applicant has further amended these claims in an effort to advance prosecution. It is respectfully submitted that the subject matter of the further amended claims, details of which are discussed below, are such that the requirements of 35 U.S.C. §112, first paragraph are met.

In particular, the claims have been amended such that the target disease is a "circulatory system disease." That is, the claims have been amended to recite "A method of treating a circulatory system disease, comprising ..." As discussed below, not only do the amendments not raise new matter, but the subject matter of the amended claims is described in the specification so as to enable its manufacture and/or use. The Examiner discusses items (a) through (f), and these items are discussed, in turn, below.

With regard to item (a) of Applicant's traversal, the invention is drawn to circulatory system disease which has been described in the application (as viewed by one unskilled in the art) as being characterized by abnormal endothelin receptor activity. In particular, the specification describes the strong vasoconstrictor activity of endothelin (page 1, lines 15-16). The specification also describes that screening for an antagonist of the endothelin receptor is useful in the search for an agent for the circulatory system (page 2, lines 18-19). As described on page 13, lines 9-11 in the specification, the present inventors have confirmed that the endothelin receptor of the present invention is highly expressed in the circulatory system, particularly in the aorta. Therefore, the present invention directed to treating diseases of the circulatory system is described in the specification and can be carried out by those skilled in the art without undue experimentation.

With regard to item (b), the Examiner admits that the screening process can be carried out by those skilled in the art based on the description provided. However, the Examiner contends that there would be no motivation or a reasonable expectation of success. On the contrary, given the specific description of endothelin with respect to cardiac activity, there is both motivation and reasonable expectation of success for those skilled in the art to conduct screening to identify an endothelin receptor antagonist for treatment of circulatory system disease.

With regard to item (c), the present inventors have confirmed, in the specification as filed, that endothelin binds to the receptor of the present invention. See, for example, page 12, line 20 in the specification. The inventors also confirmed that signal transduction takes place in cells in response to this binding. Thus, the receptor of the present invention is a receptor having a normal function.

Furthermore, the endothelin has been shown experimentally to have activity in vivo. Therefore, if some endothelins bind to the receptor in vitro, they will also logically exhibit activity in vivo. Those skilled in the art logically consider that compounds or the like having affinity to the receptor of the present invention will exhibit activity in vivo. Thus, the present invention does not require undue experimentation to those skilled in the art.

Regarding item (d), as described above, the present inventors have confirmed that endothelin binds to the receptor of the present invention in vitro. Therefore, it is clear that the receptor of the present invention functions as an endothelin receptor. Endothelin has been shown to be active in the circulatory system. Therefore those skilled in the art would have understood, without undue experimentation, the nexus between the endothelin receptor of the present invention and circulatory system diseases.

With regard to the term "abnormal," the claims have been amended such that the objection to this term is moot.

In Paragraph 17 of the Office Action, the Examiner implies that the processes involved with employing the invention are quite complex and, so, would require undue experimentation. To the contrary, though, these tasks (whether or not they are complex) are routine to those skilled in the art and can be carried out by those skilled in the art in accordance with technical common knowledge in view of the novel and inventive contribution of the present inventors, i.e. the provision of the endothelin receptor itself.

Finally, with regard to the Examiner's contentions in Paragraphs 18-20 of the Office Action (items (e) and (f), theses points are moot in view of the claim amendment to limit the claims

to treating circulatory system disease.

CONCLUSION

There are no rejections based on the prior art. In view of the above, each of the presently pending claims in this application is believed to be fully supported and in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 299002032411. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: August 5, 2003

Respectfully submitted,

By_____

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